

SCIENCE

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In This Issue

Pages 657—676

The current issues will remain at 32 pages until we are assured of a more adequate supply of paper.

The Nature and Need of Educational Research

Douglas E. Scates

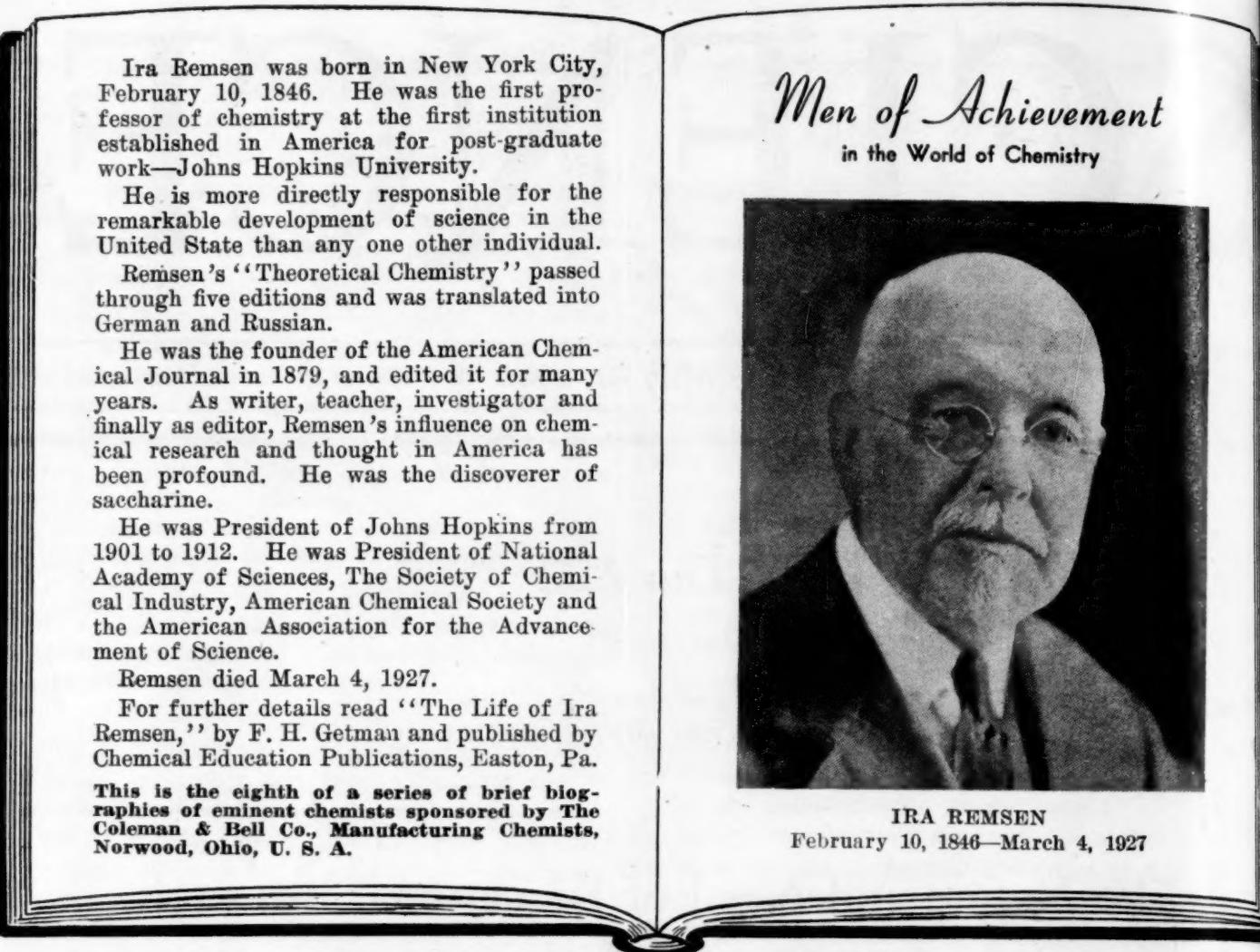
Science and Life in the World

George Westinghouse Educational Foundation Forum, 16-18 May

Technical Papers**News and Notes****Letters to the Editor****Book Reviews**

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*Published by the***American Association for the Advancement of Science**



Ira Remsen was born in New York City, February 10, 1846. He was the first professor of chemistry at the first institution established in America for post-graduate work—Johns Hopkins University.

He is more directly responsible for the remarkable development of science in the United States than any one other individual.

Remsen's "Theoretical Chemistry" passed through five editions and was translated into German and Russian.

He was the founder of the American Chemical Journal in 1879, and edited it for many years. As writer, teacher, investigator and finally as editor, Remsen's influence on chemical research and thought in America has been profound. He was the discoverer of saccharine.

He was President of Johns Hopkins from 1901 to 1912. He was President of National Academy of Sciences, The Society of Chemical Industry, American Chemical Society and the American Association for the Advancement of Science.

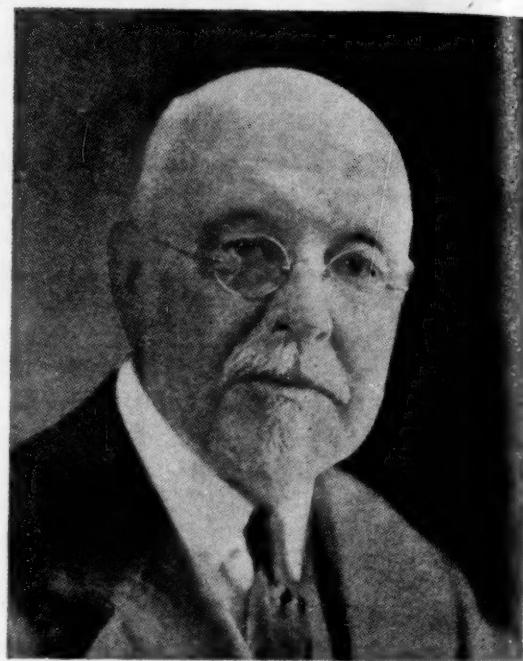
Remsen died March 4, 1927.

For further details read "The Life of Ira Remsen," by F. H. Getman and published by Chemical Education Publications, Easton, Pa.

This is the eighth of a series of brief biographies of eminent chemists sponsored by The Coleman & Bell Co., Manufacturing Chemists, Norwood, Ohio, U. S. A.

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SCIENCE

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Friday, May 31, 1946

The Nature and Need of Educational Research

Douglas E. Scates
Duke University

THE MOVEMENT FOR FEDERAL SUPPORT of scientific research began last summer with the physical sciences, but hearings before a subcommittee¹ in October made it clear that the social sciences had their own contribution to make to national welfare and security. The proposals currently being considered in the Senate and being discussed in scientific periodicals are of immediate concern to education as one of the social sciences. It is the purpose here to give a preliminary sketch of changes in the form of support for educational research which are needed if this field of research is to contribute appropriately to the progress of our society. The main problems of education cannot be solved with research facilities which are now available. Under existing conditions our central problems are not even likely to be attacked—certainly, not for a long time. Most of our research is being conducted by individuals, working usually alone and employing some procedures. The approaches to educational problems are commonly made under conditions suited to historical work and individual deliberation. The effect of these conditions on the kind of work done is to make impracticable the gathering of extensive field and laboratory data; to preclude the study of long-range growth problems; to exclude large-scale geographical problems; and to minimize the cultivation of those technical insights and sharp penetrations which come from group discussion and cooperative endeavor. The effect of these conditions on the quantity of work done is to obtain from each individual research worker only a small part of his maximum potential contribution, because of his having to do much of the work personally, and to obtain in the aggregate a quantity of educational research far below the level necessary for the proper functioning of our society.

In terms of sheer number, the large proportion of

See *Science legislation; analytical summary of testimony*. Appendix to Report from the Subcommittee on War Mobilization to the Committee on Military Affairs, U. S. Senate. Committee Monograph No. 5.) Washington, D. C.: U. S. Government Printing Office, 1945. See also *Hearings on Science legislation* (S. 1297 and related bills), which are now available in published form in five volumes.

our studies are being made by graduate students writing Masters' and Doctors' theses. And, because of the professional character of their training, they are likely to be urged to select problems having a connection with their field of practical work, rather than choose problems which are designed to test hypotheses and round out theory. Professors interested in research work diligently, possibly with some relief in their teaching schedule, but usually singlehandedly, and often with nothing whatever in the way of funds for the purpose. There are a number of research bureaus connected with higher education institutions, and these set an example which affords hope for the future; but they are far too few in number and have too small a budget. The U. S. Office of Education has been concerned largely with reports, summaries, and survey data. State and city research bureaus are concerned with immediate and usually local problems.

The great majority of persons who are interested in relatively fundamental research labor under a pattern of research support which evolved during an earlier period. We are now attempting to carry on under this pattern while living in a world of quick change, rapid progress, and tremendous competition. Our universities, largely because of financial necessity, are continuing a tradition of individual scholarship and personal research which is delightful to those who enjoy the stimulation of participating in it, but which is entirely inadequate to serve the needs of modern social progress. Our Western World is moving rapidly ahead—with our aid if we can keep up, with our hindrance if we cannot. We have recently been talking much about going forward in the postwar world; but if we are to have in this emerging period an education which is in any way distinctive, we will of necessity have an expanded and quickened research program commensurate to the task of serving an ever more intricate and kaleidoscopic civilization. There are increasingly great and increasingly acute problems which depend for solution on educational research.

There is still largely prevalent the notion that research in the social sciences is bibliographical work.

The library is a basic provision, needed in all sciences. But in those centers where social science research is being carried on vigorously it is an active, aggressive enterprise, taking its orientation not from books but from social life as it is being lived. It deals with human beings currently in action. It seeks data on the problems faced by individuals who are still looking forward. It is concerned with yesterday as a means of understanding today, and with today as a means of determining tomorrow. Students must turn to the written record to know what has previously been proposed and tried; but scientists must turn to the laboratory and to the field for fresh data and final tests.

There is on the part of many physical scientists the feeling that social problems are solely matters of conflict between interests which are to be "solved" by methods of rhetoric or the show of force. Social problems typically do involve competing sets of values, and their scientific study is likely to include certain elements which are absent from physical science. We cannot hope, and we do not wish, to make social science in all respects the same as physical science. But we can hope, and we do desire, to make social science as effective in its sphere as physical science is among physical things. We may point out that social science has been successful, in the same way that physical science has, in noting and quantifying many regularities in the realm of human living and in showing their dependence on measured amounts of conditioning factors.

On the applied side, the social and physical sciences are again similar. The physical scientist has not succeeded in eradicating friction, but he does hope to avoid explosions. So with the social scientist. In the physical field there are no fewer opportunities than in the social for the opposition of strong forces or for their dangerous disproportion. In both fields we seek forms of operation which will regularize and channel the expression of forces so that desired results may be obtained, with increasing efficiency and ever more certainty. The industrial physicist or chemist can tell management what certain amounts of certain substances will do under certain operating conditions. So the social scientist can explain to deliberative bodies the steps necessary to produce certain desired results; and knowing these things, the group can think more clearly and decide more wisely than if the issues are hazy, the elements unanalyzed, and the whole matter left to the relative effectiveness of competing vocal cords.

The social scientist must collect raw data and then analyze those data in order to produce specific or generalized truths. He commonly needs access to groups of pupils or adults, usually under specified conditions—perhaps controlled, perhaps experimental,

perhaps representing differing cultures; he needs access to tabulating and calculating machines for statistical analysis; he needs professionally trained assistants, working in something of a stable organization, to aid in carrying on the work of gathering, classifying, and analyzing large masses of data.

Let us look a little more closely at the sources of data and the kinds of problems for which they serve. Roughly, social science data lie in three directions. The first general source is the field study. This may embrace any group of persons, in this country or in other lands, representing modern or primitive cultures. Studies of how people live, grow, and implant their culture in each oncoming generation, under different physical conditions, economies, customs, ideals, provide descriptive and comparative data of great value. They reveal the existence and relative importance of factors which, under more limited conditions of observation, are either ignored or assumed not to exist. Such studies deal usually with the larger outlines of social and educational structure, giving many suggestions as to the variety of patterns which are workable, and prevent us from drawing false conclusions.

In these field studies we may be interested in general, over-all descriptions, or we may wish to single out certain factors for special study. We may make a quantitative survey for analytical, normative, or comparative purposes, or we may be concerned with the more immediate interaction between forces and their consequences, leading to causal-comparative, ecological, and correlational studies. For example, one may desire an inventory of the learning problems faced by children from bilingual homes of specified social economic levels. One may seek to ascertain what factors discourage young people of high native ability from continuing through high school and college. One may ask: "To what extent and in what ways does money pay, granted equally favorable economic conditions?"

A second source of data is the experimental study. Here we have typically the laboratory and the controlled classroom or experimental school. Data from experiments give results on principles of learning, the efficiency of different methods of teaching, on the value of different kinds of incentives, and so on. This is the type of study which, in the social sciences, corresponds most closely to typical work in the physical sciences. It is not, in our field, any more scientific than other forms of research, nor is it necessarily more valuable; each type of work is essential for one's own area of understanding. For certain social experiments it is necessary again to go into the field, since problems of morale, of loyalty, of motivation call for large groups of persons under conditions gathered

representing their ordinary walks of life but with experimental factors present.

The third large source of data in social research is the longitudinal study. This approach yields data on growth, on learning over extended periods, and on the long-time interaction of varying factors. Both normative interest and experimental attack are here represented, with another dimension—time—added in. The longitudinal approach is necessary to obtain cultural case histories, such as those needed by the physician to know the normal course of a disease, those needed by the sociologist to relate antecedents and consequents in the unfolding of delinquent and criminal careers, and those needed by the educator to ascertain whether precocious and brilliant young persons make good in later life. What are the case histories of mature personality maladjustments, what experiences lead up to them, and what are their early assumptions? How helpful are certain of our common forms of education in later life? Of those students trained in a specific vocation in high school, how many later work in that field? In addition to such cultural histories we need results of long-time experimentally controlled factors. What is the effect of a learning experiment carried out, not for three or six months, but for twelve years of elementary and high school education? Can intelligence be improved, or is it constant for a given individual? To what extent can education for specific ends be made to carry over to adult habits and community affairs?

When one compares the work necessary in gathering data from these sources with the normal classroom-class-library routine of college professors, the difficulty of doing fundamental research becomes clear. There are but few instances in the social sciences, and especially in education, where professors are given funds and other administrative concessions necessary to do anything adequate in the way of gathering and analyzing fresh data on problems of some magnitude. Individuals with scholarly inclinations do find worthwhile problems of the type and size they can attack singlehandedly; but all such problems combined and worked on indefinitely will still not make up the range of essential research, for the most fundamental problems cannot be attacked by individuals working alone. The painstaking development of insights and the thoughtful spinning of new theories are necessary and can be done in part by individuals; but such work is most prolific and helpful when it grows out and is supplemented by, a large amount of empirical study to guide thinking and to try out the generalizations being put forward. Science does not progress without imagination and venturesome suggestion, but neither does it make solid gains without gathering data to test each plausible proposal. Ra-

tionalization precedes empiricism at constant peril.

The means for bringing the routine of research-minded professors more nearly into line with the accelerated production rate demanded by modern life is to be found principally in terms of adequate funds. Colleges and universities cannot provide the money necessary to capitalize on the existing research capacities of their faculties without either increasing their income two- or threefold or greatly curtailing their teaching. To embark on the latter course at a time when our civilization is calling for more people with more education would be unreasonable. Universities must still honor their first obligation to teaching. But meanwhile society has a crying need for productive work in the social sciences which cannot be satisfied by existing patterns of research support.

The effect of liberal amounts of money on the rate of research production has been abundantly demonstrated during the recent war.² The newspapers have released accounts of many new inventions. Most outstanding is the atomic bomb which, according to newspaper reports, cost some \$3,500,000,000. In the biochemical field, a substitute for quinine is a striking example of what can be done under urgency and financial adequacy. According to reports,³ \$5,000,000 was set aside for this work, with the result that we now have several drugs *superior* to quinine in the treatment of malaria. In both of these instances, and in numerous others, the desired results were achieved because good research men were brought together, were given a liberal budget, and were told to produce. Results were demanded, paid for, and delivered.

One may reasonably ask: "Why not spend comparable sums in an effort to avoid any occasion for using the atomic bomb?" That is certainly the hope of all people. The only answer is that our society has not yet come to think in terms of social science. We have confidence in the physical and biological sciences to the extent of the expenditures reported; social science has had no such amounts given to it by which to produce spectacular results. We would not expect to get impressive returns in the physical sciences on a niggardly outlay; neither can we expect to do so in the social sciences. It is becoming literally true that society can buy almost any result it wishes; it cannot, however, do so without paying a commensurate

² It has been suggested by M. L. Tainter in "An industrial view of research trends" (*Science*, 1946, **103**, 95-99) that research productivity *per man hour* of research work during the war was not, on the average, increased. That scarcely has bearing on the fundamental point that by employing more persons more research will be undertaken and completed, and that by grouping workers and employing assistants more basic problems will be undertaken. The research program *per calendar year* was amazingly stepped up during the war.

³ Associated Press dispatch by Frank Carey, 3 January 1946. See also "Wartime research in malaria," by the Board for the Coordination of Malaria Studies (*Science*, 1946, **103**, 8-9).

price. These comments do not mean that research comes in small packets, already on a shelf, to be taken down when wanted, but they do mean that there can be great faith in the creative genius of man when his working conditions are good and when the need is urgent. We have the men; we have the need. The question is whether we shall supply the essential working conditions.

One may ask what amount of money would be called for in order to carry on the research in the social sciences needed by our society and by the world. The only correct answer is that the amount depends on the results wanted and the speed with which they are wanted. It is possible, however, to give something of a picture of the structure of research provisions which would seem, on a priori grounds, to be desirable; and it may be reasonable to make certain suggestions as to amounts that could be used to advantage under present conditions. In doing so, the present writer can give only his own ideas, and those concern only educational research; other social fields must produce their estimates of needs.

It seems clear that allowances must be thought of in terms of different levels of work, called for by different types of problems or by different degrees of intensity with which it seems desirable to pursue different problems. Normally there would be a small number of very large—or very important—problems which would demand large expenditures. These can be estimated only roughly. At any time there might be from one to half a dozen projects going forward, each of which would involve from \$75,000 to \$500,000 or more, though not necessarily this much each year.⁴ These would probably be nationwide undertakings, though not all of the survey type. There are large experiments to be undertaken, with large numbers of persons, which would be costly but are essential to social progress and control.

On a more limited level, research centers of the types which have proved so valuable in contributing to educational research in recent years should be established in some 50 to 100 places throughout the country. One need but mention the Institute of Educational Research, with its several divisions, at Teachers College, Columbia University, the Institute of Human Relations at Yale University, the Child Welfare Research Station at the State University of Iowa, and similar centers at the Universities of California, Chicago, and elsewhere, to suggest the basic importance of this organized form of research for producing vital results. It is possible also that national organizations which exist solely for the purpose of

⁴ In the 1930's the U. S. Office of Education was allotted over \$2,500,000 for five projects, and other undertakings were given from \$500,000 to \$1,000,000 each. See Carter V. Good, *Educational progress during the past year* (1937). *Sch. & Soc.*, 1938, 47, 345-352.

fostering research, such as the American Education Research Association or the Society for Research in Child Development, should have the disbursal of research funds under their control. The amount needed by each such center or agency might range from \$10,000 to \$50,000 or more per year, again depending on the kind of problems attacked and the rate of work. Centers of the types referred to, organized with some permanence, are in a position to work on long-range problems which the individual research worker cannot or will not undertake.

In addition to such research through organized staffs, the rich potentialities of individual work should be freed from the limitations which now restrict it to problems which are convenient for singlehanded attack. Professors or other qualified research workers who have problems of significance should be given the amounts that their work may demand for effective prosecution. They may need funds for travel to distant sources of data; they may need tabulating and calculating machines and skilled operators; they may need the services of research mathematicians or of consulting statisticians to design experiments or to work out new mathematical procedures appropriate to their problems; or they may need the full-time cooperation of other social scientists throughout their study. Universities may have to be reimbursed occasionally a faculty member takes off full time for the prosecution of research. These personally directed projects will call for, let us say, from \$1,000 to \$15,000 per year in each case. How many persons could use this aid in a year? We do not know in advance of trial, but if pressed for an answer, we should note that there are approximately 900 college teachers colleges, and universities in the country. At least one faculty member in every third institution would have a research bent and sufficient perspective to be ready to attack, to the advantage of our society, several problems in succession.

A rough total can be obtained from the foregoing suggestions. The maximum called for in the outline would be about \$9,000,000; the bare minimum, around \$1,000,000. The minimum of both numbers and amounts, however, would be much less than a satisfactory figure, even for a minimum estimate. These amounts seem large, they are small in comparison with the amounts spent for physical research either by the Government during the war or by industry in any year. In fact, the maximum estimate is less than the average amount by which American industry increased its research expenditures each year over the period from 1920 to 1940.⁵ A real question

⁵ Obtained from Table I, p. 80, of Vannevar Bush, *Science, the endless frontier: a report to the President*. Washington, D. C.: U. S. Government Printing Office, 1945. Estimates of Federal support needed for physical research were set at \$122,000,000 for a mature program (p. 33).

ay be raised as to whether it is sound policy to operate a public enterprise as large as the school system, costing between \$2,000,000,000 and \$3,000,000 a year, with so small an expenditure for research to regulate and guide it. The maximum estimate suggested above is 0.5 per cent of this operating expenditure.

The lay person may inquire: "What will you study, aside from trying to improve methods of teaching spelling, reading, and so on? All of us got enough of these to get along in life somehow." This type of

question has been asked countless times by practical people with respect to the physical and biological sciences during their history; it reflects simply an utter lack of understanding of science and its basic contributions. So long as nobody had ever thought of steel, iron workers wondered what physics or chemistry was good for. Before the atomic bomb, only physicists thought in terms of nuclear energy. Before medicine and public health measures had added 20 years to our lives, people thought that biological science was just a course to be taken in high school. Only persons of great vision know the future.

This is not the place for a listing of fundamental problems in education. Some have been suggested earlier. Reference to the *Encyclopedia of Educational Research* or a volume of the *Review of Educational Research* will make their nature and number

Scanning Science—

The Editor of Science: Last Wednesday, May 6th, I witnessed a very remarkable experiment with Prof. Langley's aerodrome on the Potomac River; indeed, it seemed to me that the experiment was of such historical importance that it should be made public.

I am not at liberty to give an account of all the details, but the main facts I have Prof. Langley's consent for giving you, and they are as follows:

The aerodrome, or "flying machine" in question, was of steel, driven by a steam engine. It resembled an enormous bird, soaring in the air with extreme regularity in large curves, sweeping steadily upward in a spiral path, the spirals with a diameter of perhaps 100 yards, until it reached a height of about 100 feet in the air at the end of a course of about half a mile, when the steam gave out, the propellers which had moved it stopped, and then, to my further surprise, the whole, instead of tumbling down, settled as slowly and gracefully as it is possible for any bird to do, touched the water without any damage, and was immediately picked out and ready to be tried again.

A second trial was like the first, except that the machine went in a different direction, moving in one continuous gentle ascent as it swung around in circles, like a great soaring bird. At one time it seemed to be in danger as its course carried it over a neighboring wooded promontory, but apprehension was immediately allayed as it passed 25 or 30 feet above the tops of the highest trees there, and ascending still further its steam finally gave out again, and it settled into the waters of the river, not quite a quarter of a mile from the point at which it arose.

No one could have witnessed these experiments without being convinced that the practicability of mechanical flight had been demonstrated.

Yours very truly,
Alexander Graham Bell

—22 May 1896

apparent. It may be noted here simply that education is closely related to the total success of any civilization and of any world order. The fanaticism of the Japanese and the Nazis was the product of carefully planned education. What is taught in the schools eventually determines the character and organization of the world in which we live. In this country, the curriculum and the objectives of education are, according to a democratic pattern, largely determined locally, and usually by educators. A large responsibility rests on their shoulders, and they need the findings of extensive research to guide them in their choice of materials, methods, and objectives which will help bring into reality the sort of world that exists in the hopes of the common man everywhere. It is for the purpose of enabling the schools to fulfill their obligation to a society ever struggling toward cherished, but constantly expanding, goals that educational research seeks a new pattern of support. As research workers, we speak, not for ourselves, and not primarily for our work, but for a social world better adjusted to the aspirations and satisfactions of man. We speak from the conviction that genuine progress toward this goal will come not through physical force alone, but through the far-reaching power of psychological force channeled through the social institution of education.⁶

⁶ The opportunity for all science to work together toward "a science of civilization" is presented by Ward Shepard in "Science for democracy" (*Science*, 1946, 103, 65-68).

Science and Life in the World

George Westinghouse Educational Foundation Forum, 16-18 May

THE GEORGE WESTINGHOUSE EDUCATIONAL FOUNDATION sponsored a three-day forum, in observance of the centennial anniversary of the birth of the founder of the Foundation, in Pittsburgh, 16-18 May. The general theme of the forum was: "Science and Life in the World."

The opening session, entitled "Science and Civilization," was addressed by A. V. Hill, foreign secretary of the Royal Society, London, who spoke on "Scientific Ethics." He called attention to the fact that "some might believe that it was a sign of approaching old age to have chosen 'Scientific Ethics' for a topic instead of something more practical and up to date," but he felt that all scientists, young and old, are really deeply concerned about ethics, whether they know it or not. He made his hearers feel that students of a scientific ethic have a definite advantage over the champions of other ethical systems in the universal cogency of scientific methods and results. "All sensible men everywhere finally agree about the facts; race, religion, and political opinion have no bearing at all on them or their interpretation," he concluded.

Prof. Hill went on to say:

To a cynical observer of the recent behavior of *homo sapiens* these moral reflections may sound naive: I admit that I often feel skeptical, myself, about the outcome. But there seems to be no alternative: We scientists throughout the world must take the initiative in these matters. We must not leave it to others who will certainly do nothing about it. If we do, we and our civilization may perish together.

We in England have recently watched with admiration the example of strong and courageous initiative taken by certain American scientists in refusing to be coerced and conscripted against their conscience: I say to you, the same determination exists elsewhere. As free men we are all unwilling to be used as pawns in the game of international power politics: to consent in advance to the exploitation of science for secret purposes that we may not approve.

He spoke sympathetically of the Acheson Report (*Science*, 1946, 103, 451), calling it a "notable example of the mixture of hard common-sense and practical idealism which is typical of America at its best."

In considering the subject of international control he pointed out that atomic explosions are not the only means by which a future aggressor might attempt to dominate the world. "Microbiologists," he said, "might make themselves as great international nuisances as physicists, with less danger, perhaps, of being found out in time."

Isaiah Bowman, president of Johns Hopkins University, spoke during the same session on "The Composition of Scientific Power." "We shall easily accomplish the ends of the United Nations," he said.

"Men say that world cooperation will surely work now because the swift communications of science have so obviously brought the world together." But he regretted that "our togetherness is an affair of copper wire," airplanes, and radio—technology—"rather than an affair of recognized universals of spirit and ideals."

"Our views," he held, "are no less bounded because we travel around the world swiftly, or talk to it at the instant." Even if "geographical highways" are open, psychological barriers remain.

Dr. Bowman concluded his analysis of the social composition of scientific power by saying:

Facing the raw facts of today's world we see a special role for science. If it is not yet in the area of free discussion the world around, its tendency is unremittingly international. Discussion under free conditions will help reduce the most refractory difficulties. It has been said that government, by discussion, "broke the bond of age and set free the originality of mankind." Parliament rather than dictators; free speech rather than "partisan"; rising standards of living to which applied science contributes powerfully; a striving for peace rather than a striving for confusion supported by a stimulate fear of war—these are some of the building blocks of our future "good life." Among the agencies of construction are all forms of learning, including science.

George W. Merck, president of Merck and Company, spoke realistically, factually, of biological methods of offensive and defensive warfare. He said that "in the fall of 1941 opinion in the United States regarding the possibility of biological warfare was uninformed," but that "common prudence dictated serious consideration of the dangers of possible attack along these lines."

"The President," he revealed, "directed an initiation of an extensive large-scale investigation of the possibilities and potentialities of biological warfare in the United States and the establishment of active collaboration with the British and Canadians." These objectives, he said, were attained, and "defenses against the potentially dangerous biological attacks were devised so that there was no possibility of surprise from this quarter."

He also said that, "while biological warfare was not actually used in military operations in World War II, enough was discovered to make it imperative that

use responsible for our national welfare be ever on alert in the future."

He related that "at the height of its development, the Special Projects Division of the Chemical Warfare Service of the Army, which carried the main responsibility for the biological warfare program, had personnel of 3,900. In addition, the Navy had a separate group of nearly 100 at work on a special phase of the problem. The work of these groups, and that done in the universities, research institutes, and industries, represented a truly combined operation in which Army, Navy, civilian personnel, and allied teams worked together in the closest cooperation."

The following principal accomplishments were revealed:

1. *Methods and facilities for the mass production of pathogenic microorganisms and their products were developed.* Offensively, methods were discovered for making microorganisms as virulent as possible and for maintenance of virulence under different conditions of storage or different lengths of time. Defensively, new methods for protection of personnel, animals, and plants against these virulent strains were perfected.

2. *Methods for the rapid and accurate detection of minute quantities of disease-producing agents were elaborated.* These defenses, he held, will be of value in peacetime work in laboratories, hospitals, and industries.

3. *Significant contributions were made to the knowledge of the properties and behavior of air-borne, disease-producing agents.*

4. *A pure, crystallin, bacterial toxin was isolated and studied for the first time.* This was the toxin of *Clostridium botulinum*, Type A, which, he said, "is the most potent biological poison known to man" (*Science*, 1946, 103, 613).

5. *Vaccines for the protection of chickens against two highly fatal diseases known as Newcastle disease and fowl Plague.* Chickens are an important source of food for human beings.

6. *Large-scale tests of a vaccine for the protection of cattle against rinderpest, a fatal Oriental disease, were made.*

7. *Extensive studies were made on the production and control of diseases which might affect crops of economic importance.*

8. *Information was obtained regarding the effect of more than 1,000 different chemical agents on living plants* (*Science*, 1946, 103, 469). This is a particularly fertile field that promises much to agriculture in terms of selective plant control agents, but, he said, "the work was initiated to find destructive agents against various crops and was successful." Only the rapid ending of hostilities prevented field trials in an active theater of war.

The most immediate peacetime benefit from all of this war work will be the administration, through the agency of UNRRA, of surplus rinderpest vaccine to cattle in China, where rinderpest is a disease of great

importance for the survival of the Chinese who depend on cattle for food and transportation.

At a luncheon session L. W. Chubb, director of Westinghouse Research Laboratories, spoke on "Partners in Science." He made the point that the slow methods of technological application of the past, typified by Watt and his teakettle and by Goodyear and his kitchen stove, have given way to highly specialized teams requiring great skill on the part of the individual members and long periods of training in the operations involved.

He paid tribute to the first of these partners—the scientists who are producers of new knowledge subsequently applied in industrial pursuits: he spoke of these workers as being located predominantly in the universities, where they are motivated principally by the desire for new knowledge, having in mind no immediate technological application of their work.

Dr. Chubb felt that the second "partner in science" is the inventor who suggests practical uses, new combinations, and pertinent applications of abstract knowledge passed on by the first partners.

The third partner, he said, is the engineer who develops and designs new products and processes.

He pointed out that these partnership functions need not be separated but may, occasionally, be integrated in one person, although this rarely happens. He said:

Popular opinion has put science in the saddle for several reasons. In the first place, each group of partners in science likes to think that its contribution is the most important, and I believe that the scientists and scientific journals were not at all backward in reporting their accomplishments. Then, popular reporting of scientific work is more newsy than the more prosaic work done by engineers. Finally, the most glamorous accomplishments, such as radar, the atomic bomb, and the proximity fuse, are applications of scientific knowledge more recently acquired, and they are credited mostly to the scientists, particularly physicists and chemists, who in special groups actually carried on the development. Probably well over 95 per cent of the activity on these glamorous items consisted of engineering and production. All of them were applications of prewar scientific knowledge. Although a great amount of specific research had to be done, most of the work of the scientists was invention and engineering development, and these are activities quite outside of their usual field.

He continued: "There is a general feeling that during the war a great amount of fundamental scientific work was done, and that the store of basic knowledge is full to overflowing. This, unfortunately, is not the case, because workers in pure science were taken from their usual pioneering activities and used to solve pressing war problems in industrial research, invention, and engineering development."

Now that the war is over, he said, "we need to revert to the usual sequence of technological development proven by past experience"—research scientists and professors should go back to the universities to do their chosen work in fundamental research and the training of men to carry on in industry."

In the afternoon session, "The Future of Atomic Energy," Frank B. Jewett, presiding, Robert J. Oppenheimer opened with a short address on "Atomic Explosives." One gathered that Dr. Oppenheimer was not interested in explosions, whether they were "atomic" or not.

The use of nuclear energy in warfare, he thought, should definitely be barred, but not all applications should come under the ban.

Complications come because there are perfectly legitimate ways to employ our new-found knowledge of nuclear physics. These methods need some kind of authority to guide us in applying them. At this time, he said, there is "no authority for prohibiting anything" as far as international relations are concerned.

In this connection, he spoke of his belief that the Acheson-Lilienthal Report (*Science*, 1946, **103**, 451) offered the best solution for "making use of those differences in the requirements of fissionable materials for employment in reactors as opposed to atomic explosives."

Enrico Fermi, professor of physics, University of Chicago, spoke at a later time on the uses of nuclear energy for power. He pointed out that mobile units smaller than our largest locomotives are not likely, even though the weight of the "fuel" is negligible. Massive shielding to protect operators or even casual human visitors against biologically harmful radiations is a present requirement, he said.

Speaking on the biological phase, W. Edward Chamberlain, professor of roentgenology and radiology, Temple University School of Medicine, held that the shift in emphasis from morphology to function among biologists was in part, anyway, stimulated by the discovery of the X-ray, which permitted fluoroscopic observations of function, and that the trend in this direction is now being stimulated by the availability of biological tracers and therapeutic agents manufactured in conjunction with chain-reaction piles, cyclotrons, and betatrons. He spoke in some detail on the variety of radioactive isotopes and especially of radioactive iodine in the diagnosis of pathology of the thyroid gland.

He pointed out that "therapy with radioactive isotopes is definitely a two-edged sword" and that safe procedures must be supervised by people with adequate knowledge and experience. He also felt that

supervision was going to be very difficult as radioactive materials become more generally available. One listened to his account of early X-ray abuse by the pioneers and the poorly informed, he felt that Dr. Chamberlain was warning against a too enthusiastic and misinformed use of radioactive isotopes.

In concluding, Dr. Chamberlain said that "from the point of view of biology and medicine, a truly brilliant future can be predicted for atomic energy provided its potentialities as an explosive do not lead to the total destruction of our civilization."

He went on to say: "If the greatest of physicists, chemists, and engineers can be brought together for the enterprise that made a place in history for Los Alamos, why cannot the greatest men in the fields of psychology, psychiatry, human history, and social technics be similarly brought together?"

Hugh S. Taylor, dean of the Graduate School, Princeton, spoke at this same session on the numerous chemical applications of the radioactive isotopes which now for the first time can be produced in sufficient quantities. The nuclear reactor, unlike the cyclotron, can produce useful quantities of these important tracers and possible therapeutic agents.

At the dinner session on 16 May Vannevar Bush, director of the Office of Scientific Research and Development and president of the Carnegie Institution of Washington, spoke on "Planning in Science." Excerpts from his address follow:

Do not mistake me, however, as blandly joining the chorus which is bewitched by the magic of the word "science" and sings an ill-considered and often cloying paean of praise to something summarily referred to as "the scientific method." I am decidedly not one of those who speak of the scientific method as a firm and clearly defined concept and who regard it as a mythical panacea immediately applicable to any trouble and immediately productive of complete cure. Of course, there is a system of approach to specific problems which we know as the scientific method—an orderly sequence of hypothesis and analysis which, by a series of approximations and tests, culminates in a practicable theory of operation. But to give this name of "scientific method" to mental operations involving no more than the use of common sense, or indeed to operations which are no more than rigorous logical thinking, is a mistake. I therefore wish not to be taken as joining those who facetiously argue that all we need to do to settle any difficulty is apply the scientific method to it. Nor do I wish to imply that the greater frequency which I foresee for direct intellectual contribution by scientists to our national life will consist principally in attempts to carry over into public forums, legislative committee rooms, and industrial plants a specialized technique of thinking admittedly very effective but admittedly also best suited to the laboratory and the study.

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The second day opened with a session devoted to general topic, "Transportation—A Measurement of Civilization." Edward Warner, president of the Interim Council, Provisional International Civil Aviation Organization, spoke on the aviation phase.

He said that there was no guarantee that the airplane will actually improve the world, but that it has three characteristics which give it value: (1) It gives more rapid transportation than is available by any other means; (2) it can go directly from one point to another; and (3) rising, as it does, to great heights, can give an otherwise unattainable vantage point for observation of the terrain. All of the uses to which aircraft are put arise out of some combination of these three properties. To get men together quickly may result in their quarreling, and whether or not they are going to quarrel in the future or arrive at some amicable settlement for their differences depends, the speaker said, on an understanding of the "realm of human relations." Dr. Warner said that the use of the airplane for transportation, although not limited completely to organized airlines, still, even in the future, will consist of 80 to 90 per cent of the common carrier type; and although there will be a great increase in the actual number of private planes in the United States, these will not bulk large in the percentage of total air travel.

He felt that the romantic appeal of intercontinental flight overshadows the more prosaic business of carrying day-by-day passengers between near-by points. On the airways as on the highway most travel is between adjacent points. He pointed out that, although it has been suggested that the airplane will be a factor in the enlargement of commuting areas around large cities from the present 30 or 40 miles to 100 or 200 miles, flights of this kind are still too expensive, monthly commuting ticket costing about \$200 at present rates.

In the field of international relations we run into the now familiar culture lag. In this case it seemed to the speaker a strange anomaly that, 40 years ago, crossing the Atlantic required a week, while preparation for the trip took no longer than the time required to pack a suitcase, get a ticket, and pay the fare; whereas, at the present time, when the Atlantic can be crossed in less than 12 hours, it is the very fortunate traveler who can make his way through all of the barricades of passport and visa requirements, tax receipts, and currency authorizations in less than a week of preparatory activity. The International Civilian Air Organization has to consider, among other things, the simplification of these international barriers to travel. This group believes that a passenger should not be delayed any more than 15 minutes between the time the airplane touches the ground

and the time the passenger is free to leave the port, and that a similar reasonable criterion should be applied to express shipments. The ultimate effect of international air travel will be to break down international boundaries.

The PICAQ plans a series of demonstrations of current work on air-navigation aids in the United States during this summer and will then proceed to a meeting in Montreal in September, at which it is hoped that standard systems and equipment for immediate installation can be agreed upon.

A problem for the future concerns the adaptation of radar equipment so that the pilot will himself be aware of obstacles and other aircraft instead of having to depend on radio contact with the ground station to avoid these hazards as he does today. Dr. Warner believed that it is inevitable that, step by step, the quality of air transport service will improve during the next half century and that it will become more reliable and more economical. "It will assume increasing status as a major element in the world's transportation systems. As it does, it will present new problems of organization and new problems of political and economic relationship among the nations. In its growth, it ought indeed to be a civilizing force."

Marine and rail transportation were treated by Adm. Emory S. Land, former chairman, U. S. Maritime Commission, and Martin W. Clement, president, Pennsylvania Railroad. Charles F. Kettering, general manager, General Motors Research Laboratories and chairman of the executive committee, AAAS, who was to have spoken on automotive transportation, was unable to be present, but his paper was read by A. L. Boegehold, director of the Metallurgical Department of the Research Laboratories of General Motors.

The luncheon session was addressed by Frank B. Jewett, president of the National Academy of Sciences, who spoke on "Horizons in Communications."

In the afternoon session there was a symposium on biological science, at which Cornelis B. van Niel, professor of microbiology, Stanford University, spoke on phytosynthesis, and Selman A. Waksman, professor of microbiology, Rutgers University, and discoverer of streptomycin, outlined our present understanding of microorganisms with special reference to those that are known to be either harmful or beneficial to man. Two other speakers treated biological groundwork: Linus Pauling, California Institute of Technology, spoke on "Molecular Architecture and Biological Reaction," and George W. Beadle, Stanford University, treated "High-frequency Radiation and the Gene."

The Friday evening session followed a dinner at 7:00 o'clock in the ball room of the Hotel Schenley. There were two addresses: Charles W. Kellogg, presi-

dent of the Edison Institute, spoke on "Electric Power—The Foundation of Industrial Empire," and Karl T. Compton, president, Massachusetts Institute of Technology, spoke on "Scientific and Engineering Progress—Insurance Against Aggression and Depression."

Mr. Kellogg noted that every industrial worker has the equivalent of seven horsepower of electric energy available to him, and that the electrical horsepower per man in industry grew 58 per cent in the 15-year period from 1929 to 1944. The productiveness of the individual worker is high as a result, and he can be paid more. According to Mr. Kellogg, "real wages of workers in industry grew 63 per cent in the same 15-year period." He also pointed out that workers earn, in different countries, an amount which bears a close relation to the mechanical horsepower available in these countries.

He pointed out that the first central generating station built by Thomas A. Edison in 1882 was conceived of as a means of making a filament of an electric lamp burn; the early "electric" companies were really "lighting" companies, as their names attested.

With the growth in the load on these first central stations, the use of electricity for power as well as light and the constantly increasing distance of the load from the central station, the industry encountered difficulties with transmission and distribution. With the relatively low voltage at which the direct current had to be generated for safe use by customers, substantial load growth meant either a fabulous investment in copper conductors or the necessity for many relatively small generating stations or both. This dilemma was solved by George Westinghouse, through the development of the alternating current system, which is used throughout the world today.

In 1890, Westinghouse built a small 100-horsepower, single-phase, alternating-current plant at Telluride, Colorado. The voltage was 3,000 and the transmission distance was only three miles, but the amount of copper required for the transmission line was very small compared to that needed by the direct-current plant proposed by Edison in competition. The success of this plant led to the adoption of alternating current for the first Niagara Falls plant, where Westinghouse installed three 5,000-horsepower polyphase, alternating-current generators in 1893. These machines are the forerunners of modern hydroelectric generators of well over 100,000 horsepower.

Looking back now it is easy to see that, without the alternating-current system, the size and scope of our present-day electric power systems would be quite unthinkable. The development of the years has shown the greatest economy to result from generation in large stations. Without alternating current, and consequent high

voltage for transmission, it would be impossible to carry the power away from such large stations. With the direct conveyance of power through the heaviest leather belt, travelling a mile a minute, it would require a belt nearly two-thirds of a mile wide to transmit the output from the largest modern station; but with alternating current at 220,000 volts this power can be safely carried away over three wires the size of your thumb.

In distribution throughout even urban areas, the beneficial effect of alternating current still goes marching on. At the turn of the century the high-voltage distribution about cities was at 2,200 volts. This involved only 1/10 the line loss that would occur with 220 volts, but when with the passage of time, loads became too heavy to be carried satisfactorily at 2,200 volts, substations, fed by 13,200 volt lines, were dotted about the city. Now, normal distribution is itself being stepped up to 13,200 volts with no loss in safety, with a further cut of 36-fold in line losses and the consequent ability to improve voltage regulation and to eliminate countless substances.

Dr. Compton pointed out that although the Government has called on scientists in every great emergency since the Civil War, the period between wars has been almost wholly without governmental support or recognition. In speaking about the present legislation before Congress concerning an Atomic Energy Commission, he said that, "It will be a catastrophe and a disgrace and will leave the country in a period of doldrums," if Congress should fail to pass adequate legislation at this session.

One of the objectives of the National Science Foundation legislation is to provide for, "a great program of scholarships or fellowships in order that the scientific talent inherent in the population may have full opportunity for education and demonstration, and that the deficiency in scientifically trained personnel created by our policies during the past will be eliminated." Without this provision, "laboratories will be only a delusion and a waste of money and factories will before long become obsolete."

He pointed out that labor has nothing to fear from science and that "labor has its stake" in scientific progress just as the public has.

On Friday the staff of the Buhl Planetarium and Institute of Popular Science offered two programs as alternates to the regular sessions. Both of these popular treatments were well attended by the registrants.

Saturday morning was spent in a trip through the Mellon Institute of Industrial Research under the guidance of its director, Edward R. Weidlein, who has been on its staff in several different capacities for the last 34 years.

Technical Papers

The Structure and Synthesis of the Liver *L. casei* Factor

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Several compounds have been described which are essential for the growth of *Lactobacillus casei* and which possess hematopoietic activity for animals. One of these compounds was isolated from liver and has been designated the liver *L. casei* factor (5). Another form of the compound was isolated from a fermentation product and has been termed the fermentation *L. casei* factor (3).

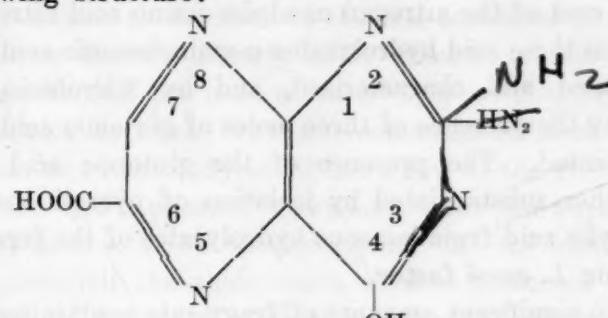
The purpose of this communication is to describe the degradation reactions used to characterize the liver *L. casei* factor and to present two methods of synthesis.

The relationship between the fermentation and the liver *L. casei* factors was shown by anaerobic alkaline hydrolysis which converted the fermentation compound into the dl-liver *L. casei* factor with the simultaneous formation of two moles of a compound which contained alpha-amino acid nitrogen.

On aerobic alkaline hydrolysis of the fermentation *L. casei* factor two fractions appeared to be formed in equimolar amounts, one of which was highly fluorescent while the other fraction gave a positive test for an aromatic amine, using the method of Bratton and Marshall (2).

The fluorescent compound was a dibasic acid having pKa values of 3.9 and 7.7. On heating the compound to 300° C., carbon dioxide was evolved, and the resulting product was a monobasic acid having a pKa of 8.0. These data indicate the presence of a monocarboxylic acid. Oxidation of the original compound with chlorine water, followed by hydrolysis with 0.1 N hydrochloric acid gave a positive test for guanidine. The ultraviolet absorption spectrum, fluorescence, empirical formula, and the formation of guanidine indicated the presence of a 2-amino pteridine containing a hydroxy and a carboxylic acid group. This substance was identified by comparison

with a synthetic compound as a pteridine having the following structure:



(I)
2-amino-4-hydroxypteridine-6-carboxylic acid

This compound was synthesized by chlorination with phosphorus pentachloride and reduction with hydrogen iodide of 2-amino-4,7-dihydroxypteridine-6-carboxylic acid (4). Evidence for the selective chlorination and reduction of the 7-hydroxy group was obtained by decarboxylation of compound (I) and the identification of the product as 2-amino-4-hydroxypteridine by comparison with a compound which was synthesized from 2,4,5-triamino-6-hydroxypyrimidine and glyoxal.

This 2-amino-4-hydroxypteridine-6-carboxylic acid can also be prepared from the corresponding 6-methyl or 6-acetic acid compound, or from the *N*-[(2-amino-4-hydroxy-6-pteridyl)methyl] pyridinium iodide by oxidation with hot alkaline potassium permanganate. These compounds are described elsewhere in this paper.

After acid hydrolysis of the aromatic amine fraction, a compound was isolated and identified as *p*-aminobenzoic acid.

Sulfurous acid cleavage of the fermentation *L. casei* factor gave a pteridine fraction and an aromatic amine. The pteridine fraction reacted rapidly with aldehyde reagents to give insoluble derivatives, which indicated the presence of a carbonyl group. The aldehyde, on standing with dilute alkali in the absence of oxygen, appears to undergo a Cannizzaro-type reaction to yield the previously described 2-amino-4-hydroxypteridine-6-carboxylic acid and another pteridine, which has been identified as 2-amino-4-hydroxy-6-methylpteridine by comparison with an authentic sample prepared by decarboxylation of 2-amino-4-hydroxy-6-pteridineacetic acid. This latter compound was prepared by the condensation of 2,4,5-triamino-6-hydroxypyrimidine and methyl γ,γ -dimethoxyacetoacetate.

Final proof that the methyl group of 2-amino-4-hydroxy-6-methyl-pteridine was in the 6-position was obtained by degradation of the compound by the

method of Weijlard, Tishler, and Erickson (6). The resulting product was compared with an authentic sample of 2-amino-5-methylpyrazine and found to be identical.

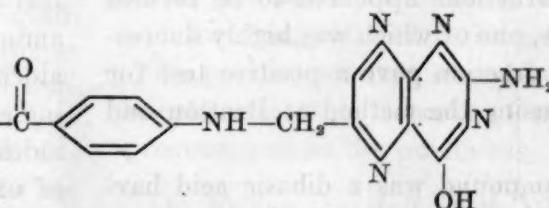
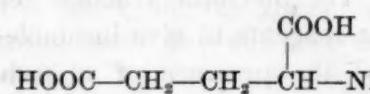
Acid hydrolysis of the amine fraction liberated 75 per cent of the nitrogen as alpha-amino acid nitrogen. From these acid hydrolysates *p*-aminobenzoic acid was isolated and characterized, and by microbiological assay the presence of three moles of glutamic acid was indicated. The presence of the glutamic acid was further substantiated by isolation of pyrrolidonecarboxylic acid from aqueous hydrolysates of the fermentation *L. casei* factor.

No significant amounts of fragments containing one or two carbon atoms could be detected in aerobic alkali or sulfuric-acid-cleaved fractions of the *L. casei* factor.

The parallel liberation of the aromatic amine and the pteridine indicated that the pteridine was attached to the amino group of the *p*-aminobenzoic acid. Since no pteridines containing more than one carbon atom in the side chain could be isolated and since there was no evidence for the existence of one or two carbon atom fragments in the hydrolysis mixtures, a one-carbon atom linkage was indicated. The necessity of oxygen for the alkaline cleavage of the *L. casei* factor suggested the presence of a methylene group. This hypothesis was further strengthened by the fact that the cleavage of *N*-benzyl-*p*-aminobenzoic acid with alkali was accelerated by the presence of oxygen.

The presence of a peptide linkage between *p*-aminobenzoic acid and glutamic acid was obvious from the liberation of alpha-amino acid nitrogen by hydrolysis of the amine fragment.

From a consideration of the above evidence, the structure indicated below was postulated for the liver *L. casei* factor.



N-[4-[(2-amino-4-hydroxy-6-pteridyl)methyl]amino]benzoyl]glutamic acid

The structure of the fermentation *L. casei* factor will be discussed in a subsequent communication.

Proof of the above structure was afforded by two methods of synthesis:

(1) The first method consisted of reacting equal molecular amounts of 2,4,5-triamino-6-hydroxypyrimidine, *p*-aminobenzoyl-*l* (+)-glutamic acid, and 2,3-dibromopropionaldehyde in the presence of an acetate buffer. The resulting crude product contained about

15 per cent by weight of the active compound as determined by microbiological assay. The condensation first gave a dihydro derivative which, during the course of the reaction, was transformed into the aromatic compound.

Purification of the active material was effected by the following procedure: The crude material was dissolved at a concentration equivalent to 400 µg. of the active compound/ml. in 0.2 N sodium hydroxide. Solid barium chloride was added to 0.2 N, and ethanol was added to a concentration of 20 per cent by volume. The precipitate was discarded. The solution was freed of barium, diluted to a concentration equivalent to 100 µg. of the active compound/ml., and adjusted to pH 7.0. The resulting precipitate was discarded and the solution was then extracted three times with 10 volume portions of butanol. The aqueous phase was concentrated to a volume equivalent to a concentration of 400 µg./ml. The solution was adjusted to pH 3.0, chilled to 0°–5° C., and the precipitate was collected. This precipitate was dissolved in 0.1 N sodium hydroxide at a concentration equivalent to 200 µg./ml. and treated with charcoal to remove any residual brown pigments. After filtration, the solution was adjusted to pH 3.0 and the active compound crystallized from hot water. This product had the physical and biological properties described in a previous publication (1).

(2) The second method of synthesis was carried out by reacting 2,3-dibromopropionaldehyde with pyridine and then condensing this product with 2,4,5-triamino-6-hydroxypyrimidine and potassium iodide to give *N*-[(2-amino-4-hydroxy-6-pteridyl)methyl] pyridinium iodide. This compound was then reacted with *p*-aminobenzoyl-*l* (+)-glutamic acid and sodium methoxide in ethylene glycol at 140° C. to give a crude product containing about 15 per cent of

the biologically active material. The active compound was purified as described above and was identical with the compound prepared by the first procedure.

By the same methods of synthesis, using *p*-aminobenzoic acid instead of *p*-aminobenzoyl-*l* (+)-glutamic acid, a compound was obtained which was active for *Streptococcus faecalis* R but inactive for *L. casei* and the chick.

For the compounds formed from *p*-aminobenzoic

acid and *p*-aminobenzoyl-*l* (+)-glutamic acid, the names pteroic acid and pteroylglutamic acid are suggested.

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Famine Edema and the Mechanism of Its Formation¹

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Edema associated with severe undernutrition was widespread in Europe during and shortly after World War I. No adequate explanation from infectious, cardiac, or renal causes was found. Speculation as to the mechanism of formation of this edema subsided with the demonstration that edema can be provoked in animals by a very low protein diet and with the accumulation of evidence for the general validity of Starling's concept of a filtration balance between hydrostatic and colloid osmotic pressures at the capillary wall. Despite some puzzling facts (10-12), by the eve of World War II there was almost universal agreement that "famine edema," as in kidney disease, is produced by a profound depression of the plasma colloid osmotic pressure, this in turn being a result of inadequate dietary protein.

In World War II, as expected, famine edema again appeared on a large scale. Contrary to expectation, however, the theory of simple hypoproteinemic causation was not fully sustained in such observations as were made (4, 7), though there was reluctance to abandon entirely this attractive theory (1, 5, 6, 9). Data gathered by the Allied Armies indicated that hypoproteinemia was common in famine areas but that it was generally slight in degree and was not closely related to the appearance or severity of edema (3, 13).

In this laboratory data were obtained from a controlled experiment with 34 men (volunteers from civilian public service), who subsisted on a European

¹This work was supported in part under the terms of a contract, recommended by the Committee on Medical Research, between the University of Minnesota and the Office of Scientific Research and Development. Substantial support was provided by the John and Mary R. Markle Foundation, the Sugar Research Foundation, the National Dairy Council, the Service Committees of the Church of the Brethren and of the Society of Friends of the Unitarian Society, and the Mennonites Central Committee. More complete acknowledgments will be made in future full publications on this experiment.

type of famine diet for six months preceded by a control period of three months and followed by three months of controlled "relief" feeding. The diet of whole cereals, potatoes, turnips, etc. provided an average of 49 grams of protein daily and proved to be closely similar to the diets in the less fortunate parts of western Europe in early 1945. These men lost an average of 24.5 per cent of their body weight. Pitting edema appeared within two months in some of the men and eventually in all but a few of the group; even the few apparent exceptions were shown, by special means, to be "waterlogged." At the end of semistarvation the thiocyanate method indicated an average SCN- space of 34.0 per cent of the total body weight and a relative excess of 7.19 kg. (15.9 lbs.) of extracellular water per man. In proportion to the non-SCN- space, the extracellular water rose from a "normal" average of 282 grams/kg. of cellular tissue to a "starvation" average of 554 grams/kg.

This development of edema was accompanied by only a small decline in plasma protein concentration, averaging 0.73 grams/100 cc. At the same time the ratio of albumin to globulin decreased to only a trivial extent. Independent analyses by the Tiselius electrophoresis method (veronal buffer) gave an average A/G of 2.00 for the heparinized plasmas of six men who showed marked edema. The same method, when applied to serum, gave A/G values of 1.70 and 1.89 for two of these men. Heparin has a slight influence on the Tiselius pattern which will be reported subsequently.

Clinical edema vanished during three months of refeeding which produced an average recovery of 37 per cent of the lost weight. At the same time the plasma protein concentration returned to normal, but there was a slight fall in A/G; by the Tiselius method A/G averaged 1.82 in the heparinized plasmas of the six men mentioned above. Clearly, the edema was not explicable in terms of hypoproteinemia or subnormal colloid osmotic pressure in the plasma, even with "correction" for protein in the interstitial fluid; edema fluid in this condition is extremely low in protein.

These subjects, like the victims abroad, showed a marked polyuria, profound bradycardia, and no rise in the concentrations of nonprotein nitrogen and chloride in the plasma. The liver was not palpable, and the heart was much diminished in size by X-ray examination. Thiamine deficiency was definitely ruled out by the analysis of food and excreta for thiamine, the reduced size of the heart, and by the absence of signs of polyneuritis. Direct measurements of venous pressure showed that, instead of an increase, there was a markedly subnormal level. At the end of semi-

starvation the mean supine venous pressure in 32 men was 4.80 cm. of saline solution with the needle in an arm vein and the manometer zero at 10 cm. above the table level. Control measurements on 12 normal men gave averages of 9.7 and 10.3 cm. on two occasions five months apart. Data on two of the subjects who showed only moderate clinical edema after six months of semistarvation are given in Table 1. During refeeding, the venous pressure gradually rose to normal values.

TABLE 1

Subject No.	Body wt. (kg.)			SCN- Space		Plasma Prot.	Ven. Press. Cm.
	Control	Starv.	Diff.	% Wt.	Edema*		
109	79.3	59.5	-19.8	31.0	5.4	6.44	1.79
112	61.4	49.0	-12.4	32.3	5.0	6.78	2.01

* The figure for "edema" represents the excess extracellular water as calculated from the proportion in the normal state.

The more prominent factors in the Starling concept of edema formation would not seem to explain famine edema unless we accept the unlikely hypothesis of a remarkable hydrostatic pressure gradient between the capillary and the larger veins. Parenthetically, it may be noted that there was a moderate arterial hypotension at both systole and diastole. Of the items in the Starling equation as elaborated by Schade and Clausen, Krogh, and others, there remains only the tissue pressure. Youmans, *et al.* (12) emphasized this neglected factor in their attempt to explain endemic edema in Tennessee, but their calculations as to the magnitude of this pressure have been properly rejected (2, 8). Although we must agree that there is great uncertainty about the actual tissue pressure at the site of filtration, normally it is probably only a small fraction of the plasma colloid osmotic pressure. From digital examination it appears that the tissue pressure in starvation is subnormal, but even a profound decline could scarcely surpass 10 per cent of the intracapillary pressure. By exclusion, then, it appears that the balance between blood plasma and interstitial fluid does not represent a simple equilibrium, as is customarily postulated.

The assumption of actual equilibrium in such a dynamic situation as that at the capillary wall would seem to be unduly optimistic on *a priori* grounds. The fact of lymph flow is itself an indication of imperfect balance. It is well known that the prediction of rates of reactions or other events in nonequilibrium states from equilibrium equations is both hazardous and complicated. There is no reason to believe that

the exchange between plasma and tissue fluid is an exception.

SUMMARY

Famine edema was produced experimentally in 34 normal men who lost a quarter of their body weight while subsisting for 6 months on a European type of semi-starvation diet. The ratio of extracellular water to cellular tissue was roughly doubled. Their clinical state closely resembled that seen in Europe in 1945. There were no signs of renal or cardiac failure. The plasma protein concentration fell only slightly and the A/G ratio remained within normal limits. The venous pressure was roughly 50 per cent below normal. Data from the field lend support to these indications that famine edema is not simply a result of hypoproteinemia or of renal or cardiac failure. It is concluded that there is a dynamic nonequilibrium state of the capillary wall and, accordingly, calculations from equilibrium equations are inadmissible.

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Antibacterial Action of Phenanthrene-related Substances

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Intrapleural injection in tuberculous empyema (some mixed infected) of a vitamin A and D concentrate, considering it as a topical application of the cod-liver oil vitamins, resulted in disappearance of the pathogenic organisms (4).

In further clinical work, vitamin D alone proved to be responsible for the antibacterial action against tubercle bacilli, *Proteus vulgaris*, *Bacillus aerogenes*, nonhemolytic streptococcus, and *Staphylococcus aureus*.

In vitro vitamin D inhibited the growth of tubercle bacilli if added (50 units/cc.) to the culture media (Hohns, Loewenstein, Coppers Potato Media). By using the plating method, *Staph. aureus*, *P. vulgaris*,

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B. aerogenes were inhibited. These clinical and laboratory findings are being reported elsewhere in detail (4, 5).

Vitamin D (activated ergosterol) is chemically ergosterol (*i.e.* characterized by the phenanthrene ring), the antirachitic property being due to intramolecular changes (1).

Since ergosterol (nonactivated) added to culture media inhibited tubercle bacilli and *Staph. aureus*, thus excluding the antirachitic factor as being responsible for the antibacterial action, we can assume that the chemical structure of vitamin D and ergosterol is responsible.

Cholesterol (a phenanthrene-related substance) added to culture media also inhibited tubercle bacilli and *Staph. aureus*.

Substances related to phenanthrene are very com-

mon in nature (e.g. sex hormones, heart glycosides, cholesterol, ergosterol, vitamin D, etc.) (2).

The substances reported here—cholesterol, ergosterol, and vitamin D—have in common the phenanthrene ring and the antibacterial action.

In vivo, in preliminary experiments, tuberculosis in guinea pigs was suppressed by injection of large doses of vitamin D (viosterol, 5,500,000 units D or more).

Bile salts are also phenanthrene related and have been known to have "bacteriostatic action on some species of microorganism" (3).

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News and Notes

Valy Menkin, assistant professor of pathology at Duke University School of Medicine, has been appointed associate professor of experimental pathology in the newly created Department of Surgical Research at Temple University Medical School, Philadelphia.

Harold Hotelling was guest of honor at a testimonial dinner given 3 May by the Statistical Techniques Group, New York Chapter, American Statistical Association. Dr. Hotelling is leaving Columbia University at the end of the academic year to become professor of mathematical statistics at the University of North Carolina.

On behalf of the Group, Helen M. Walker presented gifts to Prof. and Mrs. Hotelling. The chairman, Irving Lorge, introduced the distinguished visitors who came to honor Dr. Hotelling. Among the speakers were: P. C. Mahalanobis, of Presidency College, Calcutta, India; Stuart Rice, chairman of the Statistical Commission of the Economic and Social Council of the United Nations; and Dean Pegram, of the Graduate Faculties of Columbia University.

Prof. Hotelling reviewed the changes in statistical theory and techniques that were developed during the 15 years of his professorship at Columbia University.

Fritz Lenz, former professor of eugenics at the University of Berlin and long-time editor of the *Archiv für Rassen- und Gesellschafts-Biologie*, is at Obernfelde bei Lubbecke, not far from Osnabrück in the

British zone of occupation. All of his family survived the war.—**Paul Poponoe** (American Institute of Family Relations).

Roger Adams, head of the Chemistry Department, University of Illinois, was presented the Theodore William Richards Medal of the American Chemical Society's Northeastern Section at a meeting Thursday evening, 9 May, in Huntington Hall, Massachusetts Institute of Technology, Cambridge.

James Bryant Conant, president of Harvard University, reviewed the life and scientific achievements of Prof. Adams, who is a native of Boston and a Harvard graduate. Prof. Foster, head of the Chemistry Department in the State Teachers College, Framingham, Massachusetts, and Section chairman, presented the medal.

Norman W. Pirie, virus physiologist at the Rothamsted Experiment Station, England, is at the Worcester Foundation for Experimental Biology as a fellow of the Foundation.

Ottavio Munerati, well known for his genetical studies on sugar beets and other crops, writes that he has continued as director of the R. Stazione Experimentale di Bieticoltura at Rovigo, Italy. Dr. Munerati is anxious to renew contacts with scientists in the United States. During the war he was able to publish only one paper: "Duration of the beet

cycle" (*Monthly Bull. agric. Sci. Pract.*, 1942, **33**, 177T-214T).—*G. H. Coons* (Bureau of Plant Industry, Beltsville, Maryland).

Icie Macy Hoobler, of Detroit, director of the research laboratory of the Children's Fund of Michigan, will receive the Francis P. Garvan Medal honoring women in chemistry, it is announced by the American Chemical Society. The gold medal will be presented to Dr. Hoobler at the Society's 110th national meeting in Chicago in September.

The Garvan Medal is the latest of a long series of honors won by Dr. Hoobler, whose achievements have made her one of Detroit's outstanding scientists. She was the first woman ever to be chairman of an American Chemical Society Division, being elected to that office by the Division of Biological Chemistry in 1930, and the first woman to head a Local Section of the Society, serving as chairman of the Detroit Section in 1930. During the war Dr. Hoobler was a member of the National Research Council's Food and Nutrition Board.

Charles E. Teeter, Jr., professor of physics and chemistry at Cambridge Junior College and formerly staff member at M.I.T. Radiation Laboratory, has been appointed research associate at Boston University. He hopes to organize an acoustics research laboratory, covering the fields of supersonics and audio-acoustics.

N. P. Dubinin, professor at the Institute of Cytology of the Academy of Sciences of USSR, Oboukh Street No. 6, Moscow, USSR, has written as follows to the Department of Zoology, Columbia University:

We are badly in need of scientific literature published in the United States. You would do a tremendous favor to the science of genetics in the USSR by asking all American colleagues working in genetics, including plant and animal breeding, to send us their publications issued during the war years.

All publications should be sent directly to Prof. Dubinin.

Capt. Curtis W. Sabrosky, U. S. Public Health Service, Office of Malaria Control in War Areas, formerly assistant professor of entomology at Michigan State College, has been appointed associate entomologist in the Division of Insect Identification of the U. S. Bureau of Entomology and Plant Quarantine, Washington, D. C.

Harry Eagle has been appointed adjunct professor of bacteriology in The Johns Hopkins School of Hygiene and Public Health. Dr. Eagle will retain his active status as senior surgeon in the U. S. Public Health Service, and his laboratory will be designated

as the Laboratory of Experimental Therapeutics of the U. S. Public Health Service and The Johns Hopkins School of Hygiene and Public Health, supported jointly by the two agencies.

George W. White, professor of geology at the Ohio State University, has been appointed state geologist of Ohio. He succeeds Wilber Stout, who retired in May after having served the State Geological Survey for 35 years, the last 18 as state geologist.

S. R. M. Reynolds, Department of Embryology, Carnegie Institution of Washington, Baltimore, was elected a membre honoraire of the Société Française de Gynécologie at the meeting of this society on 21 January 1946.

William Bloom, professor of anatomy at the University of Chicago, has resigned from his position as chairman of the Department, effective 1 July 1946, at which time he will become a member of the recently established Institute of Radiobiology and Biophysics at the University. He will continue as professor in the Department of Anatomy. *Peter P. H. De Bruyn*, who has been promoted to an associate professorship, will assume the position of chairman of the Department.

Clyde Kohn, Department of Geography, Northwestern University, Evanston, is the new secretary of the National Council of Geography Teachers.

G. T. Nightingale has resigned from the Hawaiian Pineapple Company, where he has been conducting plant physiological research during the past seven and one-half years, and has accepted appointment as head of the Department of Plant Physiology at the Pineapple Research Institute of Hawaii, Honolulu 2.

Recent Deaths

Frances Louise Long, 60, formerly ecologist at the Carnegie Institution of Washington, died in Santa Barbara, California, on 17 March.

Simon Flexner, 83, director emeritus of the Rockefeller Institute for Medical Research and authority on meningitis, infantile paralysis, and dysentery, died on 2 May.

Rollin H. Stevens, 78, president of the recently organized Detroit Institute of Cancer Research, died in Detroit on 17 May.

Joseph Sergi Kasanin, director of the psychiatry department of Mount Zion Hospital and former president of the American Orthopsychiatric Association, died on 4 May in San Francisco, California. Dr. Kasanin was author of *Language and thought in schizophrenia*.

Letters to the Editor

Carbon Dioxide as an Essential Factor in the Bacterial Decomposition of Cellulose

The decomposition of cellulose by a mixed culture of *Vibrio perimastrix* (A. Alarie. Ph.D. Thesis, McGill Univ., 1945), and another unidentified bacterium has been found to take place only in the presence of carbon dioxide.

Into each of four 125-ml. flasks was measured 50 ml. of a salt solution of pH 6.7 containing: 0.5 gram Na_2HPO_4 ; 0.5 gram KH_2PO_4 ; 0.2 gram $\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$; 0.1 gram $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$; 0.1 gram NaCl ; 0.02 gram FeCl_3 ; and 1.0 gram NaNO_3 per liter of distilled water. To each flask was added 0.5 gram of Whatman No. 41 filter paper in the form of small clippings, and finally the media were sterilized and inoculated. The flasks were fitted with an inlet tube at the bottom. Two were aerated with air from which the carbon dioxide had been removed by passing first through 50 per cent potassium hydroxide and then soda lime, and two received untreated air. The temperature was maintained at 80° F., and the duration of the fermentation was eight days.

The following results are typical of several experiments:

Flask No.	Treatment	Percentage decomposition of cellulose	pH*
1	Untreated air	5.2	7.0
2	" "	6.0	7.0
3	CO_2 -free air	0	6.6
4	" "	0	6.6

* Initially pH 6.7.

The only products found were traces of unidentified acids. Viable bacteria were present only in the flasks receiving untreated air. We believe this is the first demonstration that carbon dioxide is essential for the aerobic decomposition of cellulose by bacteria.

A. S. PERLIN and M. MICHAELIS

Faculty of Agriculture (McGill University)
Macdonald College, Quebec

Use of the Shay Rat for Assay of Antiulcer Substance

Shay and his co-workers (*Gastroenterology*, 1945, 5, 43) have described a simple method for the production of gastric ulceration in the rat. These investigators suggested that their procedure might be adapted for use as a rapid assay method for any hormonal antiulcer agent. We have used their method for this purpose.

After many modifications of the procedure described by Shay, *et al.* had been tried, it was found that male rats about 60 days old and weighing 120–150 grams were most suitable. Having been raised on Purina Laboratory Chow, the rats are fasted in individual cages for 48 hours. The pylorus is then ligated under ether anesthesia and the fasting continued. Marked ulceration develops uniformly in the rumen in from seven to nine hours. This ulceration may be reduced in extent or prevented with a sufficient dose of an antiulcer substance isolated from human urine by a procedure to be described

elsewhere. The antiulcer material was administered intravenously at the time of the operation, although intra-peritoneal injection or administration by mouth sometime prior to the pylorus ligation may prove effective.

This rat preparation may also be useful for the evaluation of antisecretory as well as antiulcer agents, for Shay, *et al.* give evidence that the occurrence of gastric ulceration in their rats may be dependent on acid and pepsin secretion. For this assay of antiulcer substances it is obvious that the Shay Rat offers many advantages over dog preparations.

FRANCES PAULS, ARNE N. WICK,
and EATON M. MACKAY

Scripps Metabolic Clinic, La Jolla, California

Reprints to Denmark

Scientists in Denmark have expressed to me their regret that they do not yet receive American scientific journals regularly and that only a few of their colleagues in the United States are sending them reprints. Apparently many American scientists are not yet aware of the fact that printed matter can be sent to Scandinavian countries by ordinary mail. It would be greatly appreciated by Scandinavian scientists if their American colleagues would send them reprints of work within their special field from 1940 up to date without waiting for requests. Requests for reprints may be very much delayed, or in many cases impossible to make, because of the lack of journals since the beginning of the war.

The writer would be very much obliged if the same favor might be extended to him when, after 1 June, he takes over the Biochemistry Department of the Polytechnic Institute (Danmarks Tekniske Højskole) in Copenhagen.

HENRIK DAM

The Rockefeller Institute for Medical Research
New York City

Differentiation of Antibiotics by Resistant Strains

W. J. Robbins, at a meeting of the New York City branch of the Society of American Bacteriologists on 27 December 1945, showed that a strain of *Staphylococcus aureus* made resistant to penicillin was affected by antibiotics produced by Basidiomycetes, demonstrating that this method could be used for the differentiation of unknown antibiotics.

We had obtained from an unclassified Actinomyces an antibiotic which by bacterial spectrum showed a marked similarity to highly purified streptomycin, differing only quantitatively. Robbins' method was employed by us in an attempt to further characterize the antibiotic. For this purpose we had previously developed in our laboratory two strains of *Staph. aureus* (A.T.C.C. 6538 and F.D.A. 209) highly resistant to streptomycin. Both resistant strains were found to be as sensitive to the un-

known antibiotic as the original strains. We could thus demonstrate by this method that this unknown antibiotic was different from streptomycin in spite of their spectral similarities.

In order to ascertain the relative degree of specificity of the resistance thus obtained, we developed strains from two parent cultures which were made highly resistant to crystalline penicillin G and examined their resistance towards penicillins F and X. It was found that the "normal" *Staph. aureus* 6538 was sensitive to penicillins F, G, and X in concentrations of 0.063, 0.078, and 0.039 µg./ml., respectively, while the "resistant" strain required 0.625, 0.625, and 1.25 µg./ml. Similar results were obtained with *Staph. aureus* 209.

These results indicate that a strain with acquired resistance against one penicillin is also resistant in the same order of magnitude to the two other penicillins. Such phenomena of group resistance of the same degree have been known for a long time with substances other than antibiotics, as in the case of resistance to various sulfonamides. We have also shown group resistance against various inorganic and organic mercury compounds with a strain of *Pseudomonas aeruginosa* made resistant to merthiolate. Thus, it becomes evident that the acquired resistance of bacteria is not as specific as are immune bodies produced by chemical substances, demonstrated by Landsteiner and co-workers.

It is likely that antibiotics and other antibacterial substances of diverse chemical structure can be differentiated by this method, as shown by Robbins and ourselves. However, the fact that three different penicillins cannot be differentiated by a penicillin G resistant strain of *Staph. aureus* indicates the limitations of this technique.

Our results will be published in detail at an early date. Upon the completion of our study, P. G. Stansly, in a letter to the editor (*Science*, 1946, 103, 402) suggested the possible use of this method which has been employed by us.

P. C. EISMAN, W. S. MARSH, and R. L. MAYER
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Inc., Summit, New Jersey

Nuclear Fission Bomb as Initiator of Earthquakes

In the California earthquake of 1906 the potential energy stored was 1.7×10^{24} ergs (N. H. Heck. *Earthquakes*. Princeton, 1936); the energy liberated in the Charleston earthquake of 1886 was estimated as 1.4×10^{23} ergs. At Freehold, New Jersey in 1938, the earthquake liberated 10^{21} ergs of the energy stored in the pre-earthquake strain in the crust of the earth at that locality. This gives us the order of magnitude of potential energies expended in seismic disturbances, but it gives only a little about the magnitude of energy necessary to initiate an earthquake.

It would be safe, however, to assume that the "trigger" energy need not be more than the potential energy of the earthquake itself in order to release the seismic strain already existing. A release of "trigger" energy of more than 10^{21} ergs is likely to result in a small earthquake if the "trigger" acts at the time of relaxation

in the earth's crust and/or far away from the strain locality. Such a relaxation usually takes place shortly after a period of an excessive seismic activity. Energy amounting to 10^{25} ergs liberated at the time and at the place of maximum strain may result in a major earthquake dangerous not only to those who pull the "trigger," but also to those who have little or nothing to do with the experiment.

Early after Pearl Harbor, a plan to induce an earthquake in Japanese waters and to ruin by means of the earthquake so produced the key industrial centers of Japan was seriously considered by military and scientific authorities here. This plan was found feasible if between 3,000 and 6,000 tons of TNT were exploded near the Pacific shores of Japan. The plan was not carried out because the nuclear fission bomb was under way, and probably it was expected to prepare the bomb and release it over Japan much earlier than this actually happened.

In the artificial induction of an earthquake it is not only the quantity of energy released but the speed of its release that is of primary importance. If a line of strain stretching for hundreds of kilometers exists in the crust of the earth, a much smaller quantity of energy than 10^{25} ergs, liberated very quickly on a spot of the line, will break the equilibrium, and the crust fissure starting at the point of explosion will proceed along the line of the strain with the velocity of sound in the rock crust.

In the rupturing or faulting process of the California earthquake, the energy of 1.7×10^{24} ergs was released during several hours, perhaps days. Not more than 60 per cent of this energy was liberated within approximately nine minutes. This gives

$$\frac{1.7 \times 10^{24} \times 0.60}{9 \times 60} = 1.9 \times 10^{21} \text{ ergs/sec.}$$

as the power of the earthquake.

During the explosive decomposition of one kilogram of TNT, the quantity of energy released is 820.7 big calories, or 3.5×10^6 kilogram meters. The speed of release of TNT energy is about 0.000009 second. Therefore, the power of explosion of 5,000 metric tons of TNT is

$$\frac{3.5 \times 10^6 \times 5,000 \times 1,000 \times 9.8 \times 10^7}{9 \times 10^{-6}} = 1.9 \times 10^{25} \text{ ergs/sec.}$$

The last figure shows that the power of explosion of 5,000 tons of TNT should be sufficient to initiate an earthquake. The nuclear fission bomb released over Hiroshima was (according to published reports) equivalent to 20,000 tons of TNT. It is not clear whether the equivalent refers to the amount of energy liberated or to the power of the explosion. Even assuming that the latter variant is the correct one, the power of the nuclear fission bomb was of the order of 10^{25} ergs/sec.—amply sufficient to initiate an earthquake, if exploded on or under the surface of land or sea.

It was estimated by the author (*Earthquakes on the expanding earth*. Transactions of 1944, American Geophysical Union) that the strength of the solid shell of the earth to the depth of 60 kilometers in a section along a great circle of our planet is such that 1.5×10^{28} ergs is

necessary to crack the earth's shell into two halves three meters apart. Nuclear fission energies are approaching this critical output, and further experimenting with large nuclear fission bombs must be carried out with great precautions.

In particular this refers to the scheduled experiments to be carried out by the Navy in the mid-Pacific on a certain date in June. The author is afraid that there may be no survivors to report on the experiment if the bomb of Hiroshima-size is exploded on or under the ocean surface, and if the preceding months are below their normal seismic activity.

If a rupture in the ocean bed caused by the test is sufficiently deep and therefore hot, the flow of water into the crack and the steam formed therein will deepen and broaden the rupture. The bulge of steam may produce a seismic tidal wave which may sweep away all ships—the targets and nontargets.

Furthermore, if the nuclear fission bomb in the planned experiment is larger than that released over Hiroshima, the "mushroom" of steam and dust from the bottom of the sea may surpass that of Krakatoa in the year 1883 by many times, both in volume of the erupted matter and in the height to which it is erupted.

The solar constant was slightly affected for several decades by the dust thrown out in the Krakatoa (C. G. Abbot and F. E. Fowle. *Volcanoes and climate*. Smithsonian Misc. Collection, 1913, Vol. 60, No. 29, 15). The climate of the earth may be affected unfavorably for many decades if the quantity of dust erupted as a result of the experiment is several times that resulting from the explosion of Krakatoa.

This consideration requires an extreme cautiousness in scheduling the experiment. The strain in the earth's crust must be estimated first, and the experiment performed at the time of a minimum strain.

If all precautions are taken, this test may be of considerable value to seismology and tectonophysics. With the exact time of explosion, its energy, and location of epicenter known, the time and the path of travel of different types of seismic waves can be studied with great precision. The experiment may be especially valuable for better study of surface and shallow waves, and waves going through the core of the earth. Records of seismographs in such an accurate seismological experiment may give a better understanding of the structure of the earth's crust and its depth, thus contributing to the science of tectonophysics.

The author is especially interested in observations on the direct transverse wave (S') through the core and in the continued records for 14 days after the explosion. The absence of a focus of S' wave at the antipode of the explosion spot would favor the writer's hypothesis of a heavy gaseous core of the earth, and occurrences of excessive earthquakes during the half-lunar period after the explosion would give valuable data for evaluation of the lagging coefficient of earthquakes after the maximum strain has been reached.

ANATOL JAMES SHNEIDEROV

The Johns Hopkins University

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Book Reviews

New drugs. Arthur D. Herrick. New York: Revere Publishing Co., 1946. Pp. xiv + 303. \$4.00.

New drugs is a practicing attorney's contribution to the manufacturer's problem of how to properly launch a new drug into interstate commerce. Its title is perhaps ambiguous, leading one at first to believe that the contents deal with descriptions of new therapeutic agents.

Meeting the requirements of the Food, Drug, and Cosmetic Act is beyond the capacity of those who are not thoroughly conversant with, or who fail to comprehend in detail, its many provisions and regulations. Mr. Herrick, an expert in the field, recognized this and planned his book as a guide through the maze of legal pitfalls in the path of anyone who is introducing a new product or altering the formula or label of a drug already on the market.

The book is easy to read because of its nonlegalistic language. It covers the application of the Act to every phase of new drug qualification. The author's technic is simple. He calls attention to the problem and then details the procedure required for its solution. Since the original manuscript was read and constructively criticized by officials of the Food and Drug Administration, the stamp of authority has been doubly placed upon it.

The text begins with a discussion of the nature of the Food, Drug, and Cosmetic Act and how it is presently administered. The author points out that one of the difficulties in meeting the provisions set forth, in the first years after enactment, was a variable policy of administration. He then progresses to an examination of several facets of the definition for the term "new drug." The place of "new" devices, cosmetics, and foods under this section of the Act is clarified.

The book progresses to a discussion of the procedure envisaged by Section 505 in assuring the safety of new drugs before they can be marketed. How to apply for permission to market is carefully outlined. The detailed information asked for in the application is extensive and covers such points as methods of manufacture and control, components and composition, labeling and samples.

One of the important sections of the text treats the investigations necessary to determine safety. The author states that "naturally the principal data supporting the new drug application deals with the investigations that have been made to determine the safety of the drug for use under the conditions prescribed for it." These include laboratory observations, animal research, clinical studies, and literature surveys. The latter are of value in supporting the clinical findings of the studies specifically undertaken by the manufacturer.

Equally helpful treatment is given the problems resulting from refusal by the Food and Drug Administration to grant permission for introduction of the product into interstate commerce.

A helpful appendix brings the Act up to date and includes new state and city drug legislation. The book

closes with a statement of the official rules of the American Medical Association Council on Pharmacy and Chemistry.

This is a text that fills a definite need in the field of drug manufacturing and distribution.

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Soap in industry. Georgia Leffingwell and Milton Lesser. Brooklyn, N. Y.: Chemical Publishing Co., 1946. Pp. viii + 204. \$4.00.

The scope of this volume is much better described by the first sentence of its Introduction than by its title. Here the authors state: "This book is intended as an *indicative* rather than exhaustive survey of the industrial uses of soluble (?) soaps. . . ." To be sure, this is in reality not a book, for there is no continuity of thought or a visible plan connecting the individual chapters; rather, one gains the impression of having been presented with a conveniently bound collection of trade-journal clippings. The 23 chapters, covering 181 pages, range over the following topics (in order): Animal Husbandry, Building and Construction, Cosmetics, Dentistry, Inks and Ink Making, Insecticides, Leather, Lubricants, Milk Production, Mining and Ore Treating, Oil Production, Paints, Paper and Packaging, Plastics, Polishes and Cleaners (for wood, metal, and glass), Restaurant Sanitation, Road Building and Maintenance, Rubber Production, Textiles, Dyeing and Printing Textiles, Wool Production, Miscellaneous.

The thoroughness with which each topic has been covered may be measured to an extent by the number of literature and patent references appended. This score varies from zero for two articles to 33 for Rubber Production. It is also curious to observe that the majority of references are not much older than five years, while nearly all the "formulae" cited were probably already well known at the beginning of this century and are mostly quoted from the standard formularies.

The use of technical nomenclature is somewhat sloppy, as is apparent from the "soluble" soaps in the first sentence of the book. These really are the water-dispersible (perhaps soluble) sodium and potassium soaps of ordinary fatty acids in contrast with the more oil-soluble, multivalent metal soaps.

In view of the obvious shortcomings, such as the incompleteness of literature and patent references, not to speak of the style, this booklet will hardly be attractive to the technical and scientific worker. However, because of its many useful hints and good "sales talks" the volume will find a place in the hands of the sales personnel of the soap and detergent industry. The remarkably thorough subject index of more than 1,400 entries adds to the usefulness of this compilation.

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